

We claim:

1. An MTAP-binding agent that specifically binds to human methylthioadenosine phosphorylase (MTAP) protein in an embedded biological sample, and wherein said biological sample is not embedded in OCT compound.
2. An MTAP-binding agent according to claim 1, wherein said binding agent is an antibody.
3. An MTAP-binding agent according to claim 2, wherein said antibody is a polyclonal antibody.
4. An MTAP-binding agent according to claim 2, wherein said antibody is a monoclonal antibody.
5. An MTAP-binding agent according to claim 4, wherein said monoclonal antibody is produced by hybridoma cell line ATCC Accession No. PTA-5001.
6. An MTAP-binding agent according to claim 1, wherein said embedded biological sample is embedded in paraffin.
7. An MTAP-binding agent according to claim 1, wherein said embedded biological sample is fixed.
8. An MTAP-binding agent according to claim 1, wherein said embedded biological sample is fixed with formalin.
9. A hybridoma cell line that produces a monoclonal antibody that specifically binds to human MTAP protein, wherein said cell line has ATCC Accession No. PTA-5001.
10. A monoclonal antibody which specifically binds to human MTAP, wherein said monoclonal antibody is produced by a cell line ATCC Accession No. PTA-5001.
11. A monoclonal antibody which binds to the same human MTAP epitope as a monoclonal antibody produced by hybridoma cell line having ATCC Accession No. PTA-5001.
12. A hybridoma cell line which produces a monoclonal antibody that binds to the same human MTAP epitope as the monoclonal antibody produced by hybridoma cell line ATCC Accession No. PTA-5001.

13. A method of making an isolated hybridoma which produces an antibody useful for assessing whether an embedded biological sample comprises cells that contain human MTAP protein, which comprises: (a) immunizing a mammal using a composition comprising a human MTAP polypeptide or a fragment thereof; (b) isolating splenocytes from the immunized mammal; (c) fusing the isolated splenocytes with an immortalized cell to form a hybridoma; and (d) screening individual hybridomas for production of an antibody which specifically binds to said human MTAP protein in an embedded biological sample.

14. A method for detecting the presence or absence of human MTAP protein in an embedded biological sample which comprises:

(a) contacting the biological sample with an MTAP-binding agent that forms a binding complex with human MTAP protein if human MTAP is present in said embedded sample; and

(b) detecting the quantity of said binding complex and thereby detecting the presence of MTAP protein in the tissue sections, wherein detection of little to no binding complex is indicative of little or no human MTAP protein in said biological sample; and

wherein said biological sample is not embedded in OCT compound.

15. A method according to claim 14, wherein said MTAP-binding agent is an antibody.

16. A method according claim 15, wherein said antibody is a polyclonal antibody.

17. A method according to claim 15, wherein said antibody is a monoclonal antibody.

18. A method according to claim 17, wherein said monoclonal antibody is produced by hybridoma cell line ATCC Accession No. PTA-5001.

19. A method according to claim 14, wherein said biological sample is fixed.

20. A method according to claim 14, wherein said biological sample is embedded in paraffin.

21. A method according to claim 20, wherein said paraffin-embedded biological sample is fixed with formalin.

22. A method according to claim 15, wherein said antibody is labeled with a detectable marker.
23. A method according to claim 15, wherein said antibody is detected by:
- (1) contacting said antibody with a detectably labeled second antibody under conditions such that the second antibody binds to said antibody; and
  - (2) detecting the second antibody so bound.
24. A method according to claim 15, wherein said antibody is detected by:
- (1) contacting said antibody with a second antibody under conditions such that the second antibody binds to said antibody;
  - (2) contacting the second antibody with a detectably labeled third antibody under conditions such that the third antibody binds to the second antibody; and
  - (3) detecting the third antibody so bound.
25. A method according to claim 14, wherein said embedded biological sample is from a patient with cancer.
26. A method according to claim 25, wherein said cancer is selected from the group consisting of non-Hodgkin lymphoma, mesothelioma, a primary brain malignancy, non-small cell lung cancer, leukemia, bladder cancer, pancreatic cancer, soft tissue sarcoma, osteosarcoma, and head and neck cancer.
27. A method for detecting the presence or absence of human MTAP protein in a biological sample fixed and embedded in paraffin, which comprises:
- (a) heating the sample;
  - (b) deparaffinizing the sample;
  - (c) inducing epitope retrieval in the sample;
  - (d) incubating the sample with an MTAP-binding agent that specifically binds with human MTAP protein to form a binding complex; and

- (e) detecting the quantity of binding complex in the biological sample, wherein detection of little to no binding complex is indicative of little or no human MTAP protein in said sample.
28. A method according to claim 27, wherein said epitope retrieval is done using heat.
29. A method according to claim 28, further comprising adding a proteolytic enzyme following said heating.
30. A method according to claim 29, wherein said proteolytic enzyme is trypsin.
31. A method according to claim 27, wherein said fixed embedded paraffin sample is fixed with formalin.
32. A method of selecting a patient for treatment of an MTAP deficient cancer with a therapy regimen directed to MTAP deficient cancers, which comprises the steps of:
- (a) providing an embedded biological sample of the cancer from said patient;
  - (b) contacting said sample with an MTAP-binding agent that specifically forms a binding complex with human MTAP protein present in said sample; and
  - (c) detecting the quantity of binding complex in said sample and thereby detecting the quantity of human MTAP protein in the sample, wherein a sample having low or no detectable binding complex is indicative of a cancer amenable to treatments directed to MTAP deficient cancers.
33. A method according to claim 32, wherein said therapy regimen includes a drug that inhibits *de novo* purine synthesis.
34. A method according to claim 33, wherein said drug is L-alanosine, 10-propargyl-10-deazaaminopterin (PDX), N-(4-(((2,4-diamino-6-pteridiny)methyl)methylamino)benzoyl)-L-glutamic acid (methotrexate), AG2037 (Agouron/Pfizer), 4-aminopteroylglutamic acid (aminopterin), 2,4-diamino-5-methyl-6-[[[(3,4,5-trimethoxyphenyl)amino]methyl]quinazoline (trimetrexate), pyritrexim, 10-ethyl-deaza-aminopterin (edatrexate), 4'-methylene-10-deazaaminopterin (MDAM), 10-propargyl-5,8-dideazafolic acid (PDDF), N-[5-[N-(3,4-dihydro-2-methyl-4-oxoquinazolin-6-yl)methyl)-N-methylamino]-2-thenoyl-L-glutamic acid (raltitrexed);

ZD1694, Tomudex), *N*-[4-[2-(2-amino-3,4-dihydro-4-oxo-7*H*-pyrrolo[2,3-*d*]-pyrimidin-5-yl)ethyl]-benzoyl]-L-glutamic acid (LY231514; Lilly), 6-(2'-formyl-2'naphthyl-ethyl)-2-amino-4(3*H*)-oxoquinazoline (LL95509), (6*R,S*)-5,10-dideazatetrahydrofolic acid (DDATHF), 4-[2-(2-amino-4-oxo-4,6,7,8-tetrahydro-3*H*pyrimidino[5,4,6][1,4]-thiazin-6yl)-(S)-ethyl]-2,5-thienoylamino-L-glutamic acid (AG2034), and *N*-[5-(2-[(2,6-diamino-4(3*H*)-oxopyrimidin-5-yl)thio]ethyl)thieno-2-yl]-L-glutamic acid (AG2009), 6*R*2',5'thieryl5,10-dideazatetrahydrofolic acid (LY309887), (S)-2-[4-[N-[(3,4-dihydro-2,7-dimethyl-4-oxo-6-quinazolinyl)methyl]-N-prop-2-ynylamino]-2-fluorobenzamido]-4-(1*H*-1,2,3,4-tetrazol-5-yl)butyric acid (ZD9331), *N*-[4-[N-[(3,4-dihydro-2,7-dimethyl-4-oxo-6-quinazolinyl)methyl]-N-prop-2-ynylamino]-2-fluorobenzoyl]-L-glutamic acid (ZM214888), *N*(alpha)-[4-[5-(2,4-diaminopteridin-6-yl)pent-1-yn-4-yl]benzoyl]-*N*(delta)-hemipthaloyl-L-ornithine, or *N*(alpha)-(4-amino-4-deoxypteroyl)-*N*(delta)-hemipthaloyl-L-ornithine (PT523).

35. A method according to claim 32, wherein said MTAP-binding agent is an antibody.
36. A method according to claim 35, wherein said antibody is a polyclonal antibody.
37. A method according to claim 32, wherein said antibody is a monoclonal antibody.
38. A method according to claim 37, wherein said monoclonal antibody is produced by hybridoma cell line ATCC Accession No. PTA-5001.
39. A method according to claim 32, wherein said embedded biological sample is fixed.
40. A method according to claim 32, wherein said biological sample is embedded in paraffin.
41. A method according to claim 40 wherein said paraffin-embedded biological sample is fixed with formalin.
42. A method according to claim 32, wherein said cancer is selected from the group consisting of non-Hodgkin lymphoma, mesothelioma, a primary brain malignancy, non-small cell lung cancer, leukemia, bladder cancer, pancreatic cancer, soft tissue sarcoma, osteosarcoma, and head and neck cancer.
43. A kit for determining whether an embedded biological sample contains human MTAP protein comprising: (a) an MTAP-binding agent that specifically binds with an

embedded human MTAP protein to form a binding complex; and (b) an indicator capable of signaling the formation of said binding complex.

44. A kit according to claim 43, wherein said binding agent is an antibody.

45. A kit according to claim 44, wherein said antibody is a monoclonal antibody.

46. A kit according to claim 45, wherein said monoclonal antibody is produced by the hybridoma cell line ATCC PTA-5001.

47. A method of determining the homozygous deletion of the MTAP gene complex in a biological sample which comprises the steps of:

- (a) contacting the sample with a binding agent that specifically binds to human MTAP protein to form a binding complex; and
- (b) detecting the quantity of binding complex in the sample, wherein detection of little to no binding complex is indicative of homozygous deletion of the MTAP gene complex.

48. A method of detecting the presence or absence of human MTAP protein in a sample which comprises:

- (a) contacting said sample with a monoclonal antibody produced by hybridoma cell line ATCC Accession No. PTA-5001 or a monoclonal antibody that binds to the same epitope as the monoclonal antibody produced by hybridoma cell line ATCC Accession No. PTA-5001, wherein said monoclonal antibody specifically binds to human MTAP protein to form a binding complex; and
- (b) determining the presence or absence of said binding complex in the sample, whereby the presence of a binding complex indicates the presence of human MTAP protein in the sample.

49. A method according to claim 48, wherein said monoclonal antibody is utilized in a Western blot.

50. A method according to claim 48, wherein said monoclonal antibody is utilized in an ELISA assay.

51. A monoclonal antibody according to claim 10, wherein said antibody is immobilized onto a solid surface.
52. An MTAP-binding agent that specifically binds to human MTAP protein present in an embedded biological sample and yields a statistical score, based on staining intensities, that permits the identification of an embedded sample comprising cells homozygously deleted for the gene encoding human MTAP protein, wherein said embedded sample is not embedded in OCT compound.
53. An MTAP-binding agent according to claim 52, wherein said agent is an antibody.
54. An MTAP-binding agent according to claim 53, wherein said agent is a polyclonal antibody.
55. An MTAP-binding agent according to claim 53, wherein said agent is a monoclonal antibody.
56. An MTAP-binding agent according to claim 55, wherein said monoclonal antibody is produced by hybridoma cell line ATCC Accession No. PTA-5001.
57. An MTAP-binding agent according to claim 4, wherein said antibody has a binding affinity for said human MTAP greater than  $10^5 \text{ M}^{-1}$ .
58. An MTAP-binding agent according to claim 57, wherein said antibody has a binding affinity greater than  $10^7 \text{ M}^{-1}$ .
59. A method according to claims 17, 37, or 48, wherein said antibody has a binding affinity for said human MTAP greater than  $10^5 \text{ M}^{-1}$ .
60. A method according to claim 59, wherein said antibody has a binding affinity greater than  $10^7 \text{ M}^{-1}$ .
61. An MTAP-binding agent that specifically binds to human methylthioadenosine phosphorylase (MTAP) protein in a sample obtained from a fine-needle biopsy or fine-needle aspirate.
62. An MTAP-binding agent according to claim 61, wherein said binding agent is an antibody.

63. An MTAP-binding agent according to claim 62, wherein said antibody is a polyclonal antibody.
64. An MTAP-binding agent according to claim 62, wherein said antibody is a monoclonal antibody.
65. An MTAP-binding agent according to claim 64, wherein said monoclonal antibody is produced by hybridoma cell line ATCC Accession No. PTA-5001.
66. An MTAP-binding agent according to claim 61, wherein said sample is fixed.
67. An MTAP-binding agent that specifically binds to MTAP protein from a sample that is affixed to a slide as a smear either manually, using a ThinPrep processor, using a Cytospin apparatus, or by centrifugation techniques.
68. An MTAP-binding agent according to claim 67, wherein said binding agent is an antibody.
69. An MTAP-binding agent according to claim 68, wherein said antibody is a polyclonal antibody.
70. An MTAP-binding agent according to claim 68, wherein said antibody is a monoclonal antibody.
71. An MTAP-binding agent according to claim 70, wherein said monoclonal antibody is produced by hybridoma cell line ATCC Accession No. PTA-5001.
72. An MTA-binding agent according to claim 67, wherein said sample is from blood.
73. An MTAP-binding agent according to claim 67, wherein said sample is from bone marrow.
74. An MTAP-binding agent according to claim 67, wherein said sample is from an effusion.
75. An MTAP-binding agent according to claim 67, wherein said sample is from urine.
76. An MTAP-binding agent according to claim 67, wherein said sample is fixed.



77. A monoclonal antibody which is capable of binding human MTAP protein in an embedded biological sample wherein said biological sample is not embedded in OCT compound.
78. A monoclonal antibody secreted by a cell line deposited by ATCC Accession No. PTA-5001.
79. Functional antigen binding fragments of a monoclonal antibody secreted by ATCC Accession No. PTA-5001.
80. Functional antigen binding fragments of a monoclonal antibody which binds to the same human MTAP epitope as a monoclonal antibody produced by a cell line having ATCC Accession No. PTA-5001.